Pentraxin-3 predicts functional recovery and 1-year major adverse cardiovascular events after rehabilitation of cardiac surgery patients.

Pentraxin-3 Predicts Functional Recovery and 1-Year Major Adverse Cardiovascular Events After Rehabilitation of Cardiac Surgery Patients

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■ **BACKGROUND**: Inflammatory and vascular markers have proved to be predictors of outcome in myocardial infarction and heart failure. We evaluated several circulating markers of cardiac stress, inflammation, and endothelial function to investigate their ability to predict short-term functional recovery and long-term clinical outcome in heart surgery patients undergoing inpatient rehabilitation.

■ **METHODS**: This prospective, multicenter study enrolled 223 patients after heart surgery, included in a 3-week program of standardized and supervised physical training. The association between biomarkers (pentraxin-3 [PTX3], brain natriuretic peptide, high-sensitivity cardiac troponin-T [hs-cTnT] and C-reactive protein [hsCRP], creatine kinase, myoglobin, and urinary albumin excretion [UACR]) and exercise capacity (6-minute walk test, 6MWT) or 1-year incidence of major adverse cardiovascular events (MACE) was tested in models that included biohumoral markers, and clinical and instrumental variables.

■ **RESULTS:** The patients (69.5% men, mean age of 67 ± 11 years) were enrolled after valvular surgery (52.7%) and 58.6% after coronary artery bypass grafting (CABG). Exercise capacity improved during rehabilitation (6MWT distance from 279 ± 95 to 386 ± 91 m; $P < .0001$); concentrations of most biomarkers decreased (hsCRP: 79% [$P < .0001$]; hs-cTnT: 57% [$P < .0001$]; UACR: 36% [$P = .05$]). Among the tested markers, PTX3 showed the closest association with 6MWT distance ($P = .01$) and was the only predictor of MACE, also in the subgroup of CABG patients (OR [95% CI] = 1.14 [1.03-1.27]; $P = .015$).

K E Y W O R D S

biomarkers

cardiac rehabilitation

cardiac surgery

pentraxin-3

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The authors declare no conflict of interest.

■ **CONCLUSION:** PTX3, a marker of vascular inflammation and cardiovascular damage, is a predictor of short-term functional recovery and 1-year MACE in patients undergoing rehabilitation after cardiac surgery, regardless of clinical and instrumental parameters.

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A number of hemodynamic, remodeling, inflammatory, and vascular biomarkers, including brain natriuretic peptide (BNP), cardiac troponins, C-reactive protein (CRP), and microalbuminuria, have proved to be predictive of outcomes in patients with myocardial infarction (MI) and heart failure,[1-4] but there is still a lack of reliable outcome predictors in cardiac rehabilitation. Pentraxin-3 (PTX-3) has emerged as a new candidate marker of inflammation, infection, and cardiovascular disease.[5] The aim of this study was to investigate the predictive capacity of some hemodynamic, remodeling, inflammatory, and vascular biomarkers (in addition to the more frequently used clinical and laboratory variables) in relation to short-term functional recovery and long-term clinical outcomes in heart surgery patients attending inpatient rehabilitation centers.

METHODS

This multicenter study enrolled 223 patients undergoing rehabilitation after elective coronary artery bypass graft (CABG) and/or valve replacement or repair. The protocol was approved by the local ethics committees, and all patients gave their written informed consent. The patients were consecutively recruited at 4 cardiology rehabilitation centers of the Don Gnocchi Foundation located in Northern, Central, and Southern Italy. The exclusion criteria were contraindications to physical training and chronic hematological and immunological diseases.

Study Design

Upon study entry, a mean 9 ± 5 (SD) days after cardiac surgery, the clinical history of patients was recorded and each underwent a complete cardiac assessment, including chest radiography, electrocardiography, transthoracic Doppler echocardiography, and a 6-minute walk test (6MWT). The 6MWT,[6,7] which provides postsurgical functional information[8] that correlates with peak oxygen uptake[9] and clinical variables such as gender, age, weight, and height,[10-12] was used as a surrogate marker of short-term functional recovery. It was carried out on the basis of a standardized protocol under the supervision of trained professionals and utilizing monitoring of blood pressure, heart rate and oxygen saturation.

Venous blood and spot urine samples were collected at the beginning and end of the 3-week rehabilitation period. The rehabilitation program consisted of standardized and supervised physical training with incremental exercise (up to 30 minutes of cycling 5 times a week at 70% maximal heart rate) in accordance with the international guidelines.[13-15] The program was continued throughout the period of hospitalization depending on patient clinical condition, and for a further 6 weeks after discharge. At the end of the rehabilitation period, patients underwent a second clinical cardiac examination and repeated the instrumental tests administered at the time of enrolment; they also repeated the 6MWT.

Measurement of Circulating Biomarkers

Upon study entry, routine blood chemistry tests were integrated with measurements of various circulating biomarkers. The protocol for the collection and processing biological samples was predefined and standardized. All tests were repeated at the end of the 3-week rehabilitation program. The blood was processed to obtain plasma and serum samples that were immediately frozen and stored at −70°C until analysis. The determinations were made in a single run by central laboratory personnel blinded to the experimental groups and included brain natriuretic peptide (BNP, MEIA AxSYM-Abbott, Abbott Park, IL), high-sensitivity cardiac troponin-T (hs-cTnT, Elecsys, Roche Diagnostics, Mannheim, Germany)[16], pentraxin-3 (PTX3, ELISA based on in-house reagents[17]), high-sensitive C-reactive protein (hsCRP, turbidimetric method, Beckman Coulter DxC800, Brea, CA), myoglobin (MEIA AxSYM-Abbott), creatine kinase (CK, Rosalki enzymatic method), creatine kinase isoenzyme MB (CK-MB, MEIA Axsym-Abbott, Abbott Park, IL). Urinary albumin excretion was measured using a radioimmunoassay (coated tubes, Immunotech, Marseille, France), indexed to creatinine, and expressed as the urinary albumin-to-creatinine ratio (UACR, mg/g of creatinine).[3]

Followup

Patients were followed for 12 months after hospital discharge by means of clinic visits or telephone contacts to record any major clinical events. Major adverse cardiovascular events (MACE) were defined as the composite endpoint of death or unplanned hospital admission due to cardiac causes.

Statistical Methods

The changes in biomarker concentrations between the beginning and end of the rehabilitation period were tested using the nonparametric Sign test, and a *t* test was used to analyze the changes in the 6MWT results. The differences in baseline biomarker concentrations between the patients who underwent cardiac surgery with or without extracorporeal circulation (on- or off-pump) were tested using the nonparametric Wilcoxon Mann-Whitney test.

Univariate and multivariable linear regression models were used to evaluate the associations between the baseline variables and the 6MWT results (primary endpoint) on the assumption of the normal distribution of the 6MWT results being verified by means of graphical inspection. The clinically relevant variables of age, gender, body weight, left ventricular ejection fraction (LVEF), valvular surgery, blood hemoglobin, leukocyte count, blood glucose, and the estimated glomerular filtration rate (eGFR, calculated using the modified MDRD equation) were first evaluated by means of a univariate linear regression model, and those with a P value $< .05$ were entered in a multivariable clinical model. A second multivariable linear regression model was built using circulating concentrations of biomarkers (PTX3, hsCRP, hs-cTnT, CK, CK-MB, myoglobin, BNP, UACR) following the same procedure. The clinical variables and circulating biomarkers that were statistically significant in the univariate analysis were then combined into a final model.

The significant association between MACE (secondary endpoint) and the clinical variables (age, LVEF, eGFR) and circulating biomarkers (myoglobin, PTX3) upon univariate analyses was tested by means of multivariable logistic regression. All of the statistical analyses were made using SAS software (version 9.1: SAS, Inc, Cary, NC).

RESULTS

Table 1 shows the clinical characteristics of the 223 enrolled patients (69.5% male, mean age 67 ± 11 years); 17.6% had a history of previous MI, 9.6% heart failure, or 39.6% atrial fibrillation; 71.1% were New York Heart Association (NYHA) class II-IV; 52.7% were enrolled after valvular surgery and 58.6% after CABG (combined with valvular surgery in 25 cases). Mean LVEF at enrolment was 53.6 ± 10.5%.

Upon admission, patients had slightly elevated levels of most of the circulating biomarkers in comparison with normal reference values: 100% had PTX3 levels of more than 2.0 ng/mL, 94.1% BNP levels of more than 100 pg/mL, 94.9% hs-cTnT levels of more than 13.5 ng/L, 63.7% hsCRP levels of more than 3 mg/L, 79.3% UACR levels of more than 3 mg/g, and 20.4% high myoglobin levels (>72 µg/L for men, >51 µg/L for women). The 179 patients (82.1%) who underwent cardiac surgery with a cardiopulmonary bypass (on-pump) had high baseline levels of hs-cTnT (70 [33-155] vs 28 [16-75] pg/mL, $P = .0003$ vs off-pump surgery) and hsCRP (4.0 [2.5-6.4] vs 2.6 [1.3-3.9] mg/L, $P = .007$) but not of the other biomarkers. Figure 1 shows the differences in biomarker concentrations between the start and end of the period of rehabilitation, by which time all except CK-MB had decreased significantly, with the greatest reductions in hsCRP (79%, $P < .0001$), hs-cTnT (57%, $P < .0001$), and UACR (36%, $P = .05$).

Exercise capacity improved significantly during rehabilitation as reflected by the increase in the distance of the 6MWT from 279 ± 95 m at the start of the program to 386 ± 91 m at the end ($P < .0001$). We next identified the clinical variables associated with the results of the 6MWT at the end of the rehabilitation period. Univariate analysis showed that an advanced age, a reduced LV ejection fraction and reduced renal function (eGFR) were all independently associated with a shorter distance (Table 2), as were higher admission levels of the biomarkers PTX3 ($P = .003$), BNP ($P = .04$), and myoglobin ($P = .05$) (Table 3). Only PTX3 remained a statistically significant predictor in a multivariable model including the three markers ($P = .01$). PTX3 was also marginally associated with the outcome of rehabilitation in a final model that included the significant clinical predictors and biomarkers ($P = 0.07$, Table 4).

Twenty-four patients (11.9%) experienced a MACE after a median followup of 360 (298-381) days: 20 underwent an unplanned hospital admission due to cardiac causes, and the remaining 4 died (1.8%). Upon admission, these patients were older (72 ± 9 vs 67 ± 11 years) and had a lower LVEF (49.5 ± 10.5 vs 54.2 ± 10.1%) and eGFR (63 ± 27 vs 75 ± 23 mL/min/1.73 m^2) than the event-free patients. They also had higher baseline plasma concentrations of myoglobin (median [Q1-Q3] = 45 [31-61] vs 29 [24-41] µg/L) and PTX3 (median [Q1-Q3] = 12.4 [10.2-18.9] vs 9.4 [6.6-12.4] ng/mL). Univariate analysis showed that the risk of MACE was greater in the more elderly patients (OR [95% CI] = 1.05 [1.00-1.10]; $P = .04$), those with a reduced LVEF (OR [95% CI] = 0.96 [0.92-1.00]; $P = .04$), or reduced renal function (OR [95% CI] = 0.98 [0.96-1.00]; $P = .02$), and those with higher baseline concentrations of myoglobin (OR [95% CI] = 1.03 [1.01-1.05]; $P = .002$) and PTX3 (OR [95% CI] = 1.15 [1.07-1.23]; $P = .0002$). However, the only variables directly associated with MACE in a multivariate logistic model that included the clinical variables and biomarkers were higher baseline levels of PTX3 (OR [95% CI] = 1.13

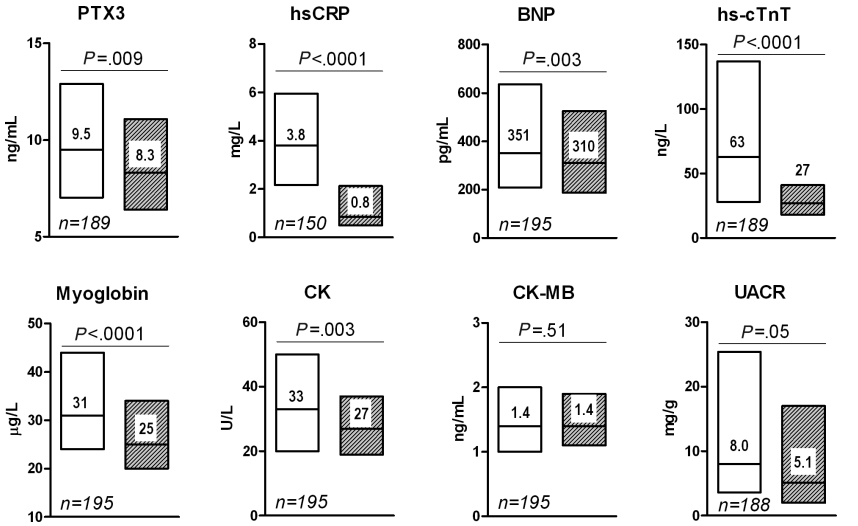

Figure 1. Box plots showing the median concentrations (inside the boxes) and interquartile ranges of the biomarkers upon admission (white boxes) and at the end of the rehabilitation period (shaded boxes); the groups were compared using the Sign test. Abbreviations: BNP, brain natriuretic peptide; CK, creatine kinase; CK-MB, creatine kinase isoenzyme MB; hsCRP, high-sensitivity C-reactive protein; hs-cTnT, high-sensitivity cardiac troponin T; PTX3, pentraxin-3; UACR, urinary albumin-to-creatinine ratio.

[1.05-1.22]; $P = .0009$) and myoglobin (OR [95% CI] = 1.02 [1.004-1.04]; $P = .02$; Table 5).

Similar analyses were made of the subgroup of 130 patients undergoing rehabilitation after elective CABG (58.6% of the total study sample). Their mean age was 68 ± 10 years; 18.5% were females; 26.9% had a history of MI (36.2% atrial fibrillation); 68.0% were prescribed a beta-blocker, 54.3% an angiotensin-converting enzyme inhibitor or an angiotensin receptor blocker, and 59.4% a statin. In these patients, only age (beta-estimate [SE] = (2.17 [0.92], $P = .02$, multivariable linear regression model) and LVEF (1.99 [0.74], $P = .009$) were significantly associated with 6MWT at the end of the rehabilitation period, but none of the assayed circulating biomarkers. On the contrary, baseline PTX3 concentration was the only variable associated with MACE in the patients with CABG (OR [95% CI] = 1.14 [1.03-1.27], $P = .015$, multivariable logistic regression model).

Table 1 • Baseline Clinical Characteristics of the Study Population

Variable	n (%) or Mean ± SD
N	223 (100%)
Age, y	67 ± 11
Females	68 (30.5%)
Body weight, kg	73 ± 16
History of myocardial infarction	39 (17.6%)
History of heart failure	21 (9.6%)
Coronary artery bypass graft	130 (58.6%)
Valvular surgery	117 (52.7%)
Left ventricular ejection fraction, %	53.6 ± 10.5
6-minute walk test, m	274 ± 97
Laboratory tests	
Hemoglobin, g/dL	10.8 ± 1.4
Leukocytes, $10^3/mm^3$	9.17 ± 2.70
Serum creatinine, mg/dL	1.09 ± 0.39
eGFR, mL/min/1.73 m^2	73 ± 24
Blood glucose, mg/dL	107 ± 33

Abbreviation: eGFR, estimated glomerular filtration rate.

DISCUSSION

The results of this study confirm that clinical data such as age, LV ejection fraction, and renal function are reliable predictors of postrehabilitation functional recovery and 1-year outcomes in patients who have undergone cardiac surgery. However, the original finding is that, considering a panel of hemodynamic, remodeling, inflammatory and vascular biomarkers, pentraxin-3 is an independent predictor of short-term functional recovery after an inpatient cardiac rehabilitation program and, together with myoglobinemia, a predictor of the long-term MACE rate.

Pentraxins are a super family of conserved, multifunctional acute-phase reactants that play a key role as effectors and modulators of innate resistance in animals and humans.[18] PTX3 was first identified as an early gene in vascular endothelial cells and monocytes that is induced in response to proinflammatory cytokines or stimulation with microbial components,[19] although it can also be produced by a variety

Table 2 • Clinical Determinants of 6MWT at the End of the Rehabilitation Period

	Univariate Model			Multivariable Model		
Variable	**Estimate (SE)**	***t* Value**	***P* Value**	**Estimate (SE)**	***t* Value**	***P* Value**
Age	−3.54 (0.55)	−6.41	<.0001	−2.71 (0.62)	−4.36	<.0001
Gender	14.09 (14.60)	0.96	.34			
Body weight	−0.11 (0.41)	−0.27	.78			
LV ejection fraction	2.47 (0.61)	4.08	<.0001	2.26 (0.55)	4.10	<.0001
Valvular surgery	18.48 (13.12)	1.41	.16			
Hemoglobin	2.18 (4.89)	0.45	.66			
White blood cell count	0.001 (0.003)	0.58	.57			
Blood glucose	−0.07 (0.20)	−0.36	.72			
eGFR	1.47 (0.26)	5.65	<.0001	0.68 (0.29)	2.35	.02

Abbreviations: eGFR, estimated glomerular filtration rate; LV, left ventricular; 6MWT, 6 minute walk test.

of other cells, including smooth muscle cells and fibroblasts.[20]

In addition, neutrophils contain a store of mature protein in their specific granules and can promptly release the molecule in response to proinflammatory signals.[21] Pentraxin is also expressed in cardiac tissue after MI,[17-22] and its plasma concentration predicts cardiovascular morbidity and mortality in patients with unstable angina,[23] MI,[24] or heart failure.[25]

As expected, we found that patients admitted to a rehabilitation program after cardiac surgery presented with high concentrations of the biomarkers related to cardiac stress or injury (brain natriuretic peptide, cardiac troponin-T, creatine kinase, and myoglobin), generalized inflammation and vascular injury (C-reactive protein and pentraxin-3), and early renal glomerular dysfunction (albumin urinary excretion), but the marked decrease in biomarker levels during rehabilitation supports the global effectiveness of even short-term programs.

Neurohormonal activation has been documented in most candidates for cardiac rehabilitation, be they patients with a recent MI or chronic heart failure, as well as patients undergoing cardiovascular surgery. The cardioprotective mechanisms evoked during a program of cardiac rehabilitation include slowing the progression or reducing the severity of coronary atherosclerosis (improved endothelial function), decreasing chronic inflammation, ensuring moderate losses of body weight and improved metabolic control (lipid and insulin sensitivity), ischemic preconditioning of the myocardium, and favorable hemostatic effects.[26-27]

To the best of our knowledge, this is the first study showing a reduction in PTX3 and hs-cTnT levels, and the UACR in such patients. Very few studies have monitored the activation of circulating biomarkers in patients admitted to cardiac rehabilitation, and these have mainly involved small series of patients with heart failure and led to conflicting results. A recent study of 95 heart failure patients found that 9 months of aerobic training significantly reduced the plasma concentrations of BNP and norepinephrine,[28] and a study of 44 MI patients enrolled in an exercise-based rehabilitation program also found a reduction in BNP levels;[5] conversely, a study of physical training involving

Table 3 • Biomarkers Associated With 6MWT at the End of the Rehabilitation Period

	Univariate Model			Multivariable Model		
Biomarker	**Estimate (SE)**	***t***	***P* Value**	**Estimate (SE)**	***t***	***P* Value**
hs-CRP	−1.04 (2.63)	−0.40	.69			
PTX3	−3.49 (1.16)	−3.02	.003	−3.02 (1.18)	−2.55	.01
BNP	−0.032 (0.016)	−2.04	.043	−0.024 (0.016)	−1.52	.13
hs-cTnT	0.011 (0.051)	0.22	.83			
CK	0.38 (0.23)	1.64	.10			
CK-MB	−1.19 (2.44)	−0.49	.63			
Myoglobin	−0.70 (0.35)	−2.00	.047	−0.51 (0.35)	−1.44	.15
UACR	−0.0091 (0.0385)	−0.24	.81			

Abbreviations: BNP, brain natriuretic peptide; CK, creatine kinase; CK-MB, creatine kinase isoenzyme MB; hsCRP, high-sensitivity C-reactive protein; hs-cTnT, high-sensitivity cardiac troponin T; PTX3, pentraxin-3; 6MWT, 6 minute walk test; UACR, urinary albumin-to-creatinine ratio.

Table 4 • Clinical and Biohumoral Determinants of 6MWT at the End of the Rehabilitation Period[a]

Variable	Estimate (SE)	*t*	*P* Value
Age	−2.53 (0.63)	−4.00	<.0001
LV ejection fraction	2.12 (0.58)	3.65	.0003
eGFR	0.67 (0.31)	2.15	.03
PTX3	−1.94 (1.08)	−1.80	.07
BNP	−0.0013 (0.0144)	−0.09	.93
Myoglobin	−0.089 (0.331)	−0.27	.79

[a]Multivariable model.
Abbreviations: 6MWT, 6-minute walk test; BNP, brain natriuretic peptide; eGFR, estimated glomerular filtration rate; LV, left ventricular; PTX3, pentraxin-3.

43 patients with heart failure found no reduction in plasma natriuretic peptide (ANP and BNP) concentrations.[29] Another study of 277 patients with coronary heart disease found that completing a 3-month formal program of cardiac rehabilitation and exercise training significantly reduced the plasma levels of CRP (a nonspecific marker of inflammation), regardless of the use of statins or weight loss.[30] Circulating CRP and fibrinogen levels were similarly reduced in 224 patients with acute MI or undergoing CABG randomized to an expanded cardiac rehabilitation program or usual rehabilitation.[31]

Even fewer studies have investigated the usefulness of cardiac biomarkers as early predictors of outcome, although it was found that initial plasma BNP levels and an anterior MI predicted left ventricular remodeling in 72 patients enrolled in a 12-week program of cardiac rehabilitation.[32] We found that PTX3,

Table 5 • Clinical and Biohumoral Determinants of Major Adverse Cardiovascular Events (MACE) at the End of the 1-Year Followup Period

	Univariate Logistic Model			Multivariate Logistic Model		
Variable	OR	95% CI	*P* Value	OR	95% CI	*P* Value
Clinical variables						
Age	1.049	1.002-1.098	.042	1.023	0.968-1.080	.417
Gender	1.184	0.465-3.013	.724			
Body weight, kg	0.976	0.945-1.007	.125			
LV ejection fraction	0.960	0.924-0.998	.041	0.960	0.922-1.000	.050
Valvular surgery	1.117	0.475-2.627	.800			
Hemoglobin	0.734	0.510-1.056	.096			
White blood cell count	1.000	1000-1.000	.948			
Blood glucose	0.997	0.983-1.012	.701			
eGFR	0.976	0.957-0.996	.020	0.980	0.957-1.004	.102
Biohumoral markers						
Hs-CRP	1.022	0.843-1.241	.822			
BNP	1.000	1.000-1.000	.207			
CK	1.004	0.992-1.017	.510			
CK-MB	1.093	0.998-1.197	.056			
Myoglobin	1.029	1.011-1.047	.002	1.023	1.004-1.043	.018
hs-cTnT	1.002	0.999-1.004	.223			
PTX3	1.148	1.067-1.234	.0002	1.132	1.052-1.218	.0009
Microalbuminuria	1.001	1.000-1.003	.1082			
Clinical variables and biohumoral markers						
LV ejection fraction				0.966	0.923-1.011	.139
Myoglobin				1.02	1.004-1.04	.016
PTX3				1.13	1.05-1.22	.0009

Abbreviations: BNP, brain natriuretic peptide; CK, creatine kinase; CK-MB, creatine kinase isoenzyme MB; eGFR, estimated glomerular filtration rate; hsCRP, high-sensitivity C-reactive protein; hs-cTnT, high-sensitivity cardiac troponin T; LV, left ventricular; PTX3, pentraxin-3.

BNP, and myoglobin were the strongest predictors of functional capacity among a panel of tested biomarkers. However, only PTX3 was marginally associated with 6MWT distance in a multivariable model that also included the most robust clinical variables (age, eGFR, and LV ejection fraction). It is very interesting to note that PTX3 levels also predicted the occurrence of MACE, a finding that has not been previously published and merits further study. Furthermore, PTX3 was a better predictor of functional recovery and 1-year outcome in postcardiac surgery patients than other robust and cardiac-specific markers such as natriuretic peptides or troponin. Similar data have been reported in relation to acute MI: day 0-1 PTX3 levels (but not NT-proBNP, CK, or cTnT levels) predicted 3-month mortality in 748 MI patients.[25]

We observed a significant difference in the predictive value of CRP and PTX3. As CRP is produced by the liver in response to IL-6 and PTX3 is locally produced in the tissues by a variety of cell types in response to primary inflammatory signals, high concentrations of circulating PTX3 probably reflect the local activation of inflammation and tissue damage. This would at least partially explain the association between plasma PTX3 levels and rehabilitative outcome in cardiac surgery patients. In addition, it has recently been found that pentraxin predicts higher hospital mortality in patients with severe traumatic brain injury,[33] that it is a useful marker of severe disease in febrile patients attending an emergency department,[34] and that it predicts of cognitive impairment in elderly hypertensive patients.[35]

In the absence of previous evidence concerning the role of PTX3 in exercise training or rehabilitation, this may simply be because the complexity and integration of the physiological mechanisms involved in functional recovery after cardiac surgery is better reflected by a molecule that is largely produced by activated endothelial cells. Once again, it is worth noting that the circulating biomarkers that were more greatly reduced after rehabilitation (hsCRP, hs-cTnT, and UACR) did not seem to be independent predictors of the 6MWT results.

LIMITATIONS

There are some limitations to this study. First of all, all of the postcardiac surgery patients were inpatients, and it is not possible to extrapolate the evolution and prognostic value of circulating biomarkers in subjects not admitted to a rehabilitation unit. Moreover, for ethical reasons, the study was designed as an observational study. Secondly, as the number of patients/events is limited, the risk of model overfitting cannot be completely ruled out. Finally, the study was not designed to evaluate the cost-effectiveness of using circulating biomarkers for risk stratification in cardiac rehabilitation. However, in the absence of conclusive data in this area, it may be considered reassuring to point out that the inexpensive measurement of a single biomarker of vascular inflammation and injury helped clinicians to predict short-term functional recovery and long-term cardiovascular events in our study population. The strength of the study lies in its multicenter prospective design and the fact that it investigated novel cardiac biomarkers in a relatively large number of patients.

CONCLUSIONS

The results of the study confirm that clinical and instrumental parameters (age, LV ejection fraction, eGFR) are reliable predictors of functional recovery in cardiac surgical patients admitted to a program of cardiac rehabilitation. In addition to robust clinical variables, PTX3 (a pleiotropic marker of vascular inflammation and cardiovascular system damage) is an independent predictor of short-term functional recovery, and the baseline concentration of PTX3 was the only variable associated with the 1-year MACE rate in our CABG patients. Given the widespread interest in biomarkers in cardiology and the paucity of evidence in the field of rehabilitation, there is a clear need for well-designed clinical studies aimed at improving our understanding of their role in cardiac rehabilitation. Whether knowledge of the circulating concentrations of PTX3 may help to stratify surgical patients referred for rehabilitation and predict their outcome needs to be confirmed.

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